CLAIMS

1. A method of inhibiting apoptosis in a hematopoietic stem cell (HSC) comprising contacting said cell with a caspase inhibitor in an amount sufficient to inhibit apoptosis in said cell.

2. The method of claim 1, wherein apoptosis is induced by ionizing radiation.

3. The method of claim 2, wherein said HSC is contacted with said ionizing radiation before said caspase inhibitor.

4. The method of claim 3, wherein said HSC is contacted with said caspase inhibitor about 4 hours after receiving said ionizing radiation.

5. The method of claim 2, wherein said HSC is contacted with said ionizing radiation after said caspase inhibitor.

6. The method of claim 5, wherein said HSC is contacted with said caspase inhibitor about 2 hours before to receiving said ionizing radiation.

7. The method of claim 1, wherein said caspase inhibitor is contacted with said HSC more than one time.

8. The method of claim 2, wherein said caspase inhibitor is administered both prior to and after ionizing radiation is contacted with said HSC.

9. The method of claim 1, wherein said caspase inhibitor is z-VAD, BocD, LY333531, casputin, Ac-DQMD-CHO, CV-1013, VX-799, Ac-YVAD-CMK, IDN-5370, IDN-6556, IDN-6734, IDN-1965, IDN-1529, z-VAD-fmk, z-DEVD-cmk, Ac-YVAD-fmk, z-Asp-Ch2-DCB, Ac-IETD, Ac-VDVAD, Ac-DQMD, Ac-LEHD, or Ac-VEID.

10. The method of claim 1, wherein said HSC is contacted with a second agent.

11. The method of claim 10, wherein said second agent is a second caspase inhibitor.

12. The method of claim 10, wherein said second agent is a radioprotectant.

13. The method of claim 11, wherein said second agent is an anti-apoptotic protein, a cytokine or growth factor.

14. The method of claim 13, wherein said anti-apoptotic protein, cytokine or growth factor is expressed in said HSC from a recombinant expression vector.

15. The method of claim 14, wherein said expression vector is a viral vector.

16. The method of claim 14, wherein said expression vector is a non-viral vector.

17. A method of inhibiting radiation-induced injury in a subject comprising administering to said subject a caspase inhibitor in an amount sufficient to inhibit radiation-induced injury.

18. The method of claim 17, wherein said caspase inhibitor is administered orally or by injection.

19. The method of claim 17, wherein said caspase inhibitor is z-VAD, BocD, LY333531, casputin, Ac-DQMD-CHO, CV-1013, VX-799, Ac-YVAD-CMK, IDN-5370 IDN-6556, IDN-6734, IDN-1965, IDN-1529, z-VAD-fmk, z-DEVD-cmk, Ac-YVAD-fmk, z-Asp-Ch2-DCB, Ac-IETD, Ac-VDVAD, Ac-DQMD, Ac-LEHD, or Ac-VEID.

20. The method of claim 17, further comprising administering to said subject a second agent.

21. The method of claim 20, wherein said second agent is a second caspase inhibitor, an anti-apoptotic molecule, a radioprotectant, a cytokine, or a growth factor.

22. The method of claim 20, wherein said second agent is an anti-apoptotic protein.

23. The method of claim 22, wherein the anti-apoptotic protein is selected from the group consisting of a p53 inhibitor, Bcl-X_L, Bcl-2, c-IAP1, c-IAP2, and XIAP.

24. The method of claim 20, wherein said second agent is a cytokine.

25. The method of claim 24, wherein said cytokine is IL-1, IL-2, IL-3, IL-4, IL-5, IL-6, or IL-7.

26. The method of claim 20, wherein said second agent is a growth factor.

27. The method of claim 26, wherein said growth factor is Flt3 ligand, c-Kit ligand, M-CSF, GM-CSF, G-CSF, VEGF, erythropoietin, or leukemia inhibitory factor.

28. The method of claim 20, wherein said second agent is a radioprotectant.

29. The method of claim 28, wherein said radioprotectant is amifostine, vitamin E, vitamin C, selenium, melatonin, 5-androstenediol, cucumin, α-phenyl-tert-butylnitrone, a flavinoid, or a nitroxide.

30. The method of claim 22, wherein said anti-apoptotic protein, cytokine or growth factor is expressed from a recombinant expression vector encoding said anti-apoptotic protein and an HSC-selective promoter.

31. The method of claim 17, wherein said caspase inhibitor is provided prior to exposure to radiation.

32. The method of claim 17, wherein said caspase inhibitor is provided following exposure to radiation.

33. The method of claim 32, wherein said caspase inhibitor is provided about four hours or less following exposure to radiation.

34. The method of claim 32, wherein said caspase inhibitor is administered more than once.

35. The method of claim 32, wherein said caspase inhibitor is provided via continuous infusion.

36. A method of screening a caspase inhibitor for its ability to inhibit radiation-induced injury comprising:

(a) providing a hematopoietic stem cell (HSC);

(b) contacting said HSC with a dose of ionizing radiation sufficient to induce apoptosis in said HSC;

(c) contacting said HSC with said caspase inhibitor; and

(d) assessing one or more apoptotic characteristics in said HSC,

wherein a reduction in the number or extent of apoptotic characteristics in said HSC, as compared to an HSC not treated with said caspase inhibitor, identifies said caspase inhibitor as an inhibitor of radiation-induced injury.

37. The method of claim 36, wherein said method comprises the use of multiple HSCs, and assessing comprises measuring the number of said HSCs undergoing apoptosis.

38. The method of claim 37, wherein assessing comprises TUNEL assay, Annexin V-7AAD or PI staining, sub G0/1 cell analysis, or caspase activity assay.

39. The method of claim 37, wherein assessing comprises flow cytometry that can discriminate between $Lin^- Sca1^+ c\text{-}kit^+$, $Lin^- Sca1^- c\text{-}kit^+$, $Lin^- Sca1^+ c\text{-}kit^-$, and $Lin^- Sca1^- c\text{-}kit^-$ cells.

40. The method of claim 36, wherein at least steps (b) and (c) are performed *in vivo*.

41. The method of claim 36, wherein said HSC is isolated and at least steps (b) and (c) are performed *in vitro*.

42. The method of claim 36, wherein said characteristics of apoptosis comprise Annexin-V staining, caspase activation, and/or DNA fragmentation.

43. The method of claim 36, further comprising contacting said HSC with a second agent.

44. The method of claim 43, wherein said second agent is selected from the group consisting of an anti-apoptotic molecule (a p53 inhibitor or an anti-apoptotic protein, such as Bcl-X_L, Bcl-2, c-IAP1, c-IAP2, and XIAP), a radioprotectant (amifostine, vitamin E, vitamin C, selenium, melatonin, 5-androstenediol, cucumin, α-phenyl-tert-butylnitrone, a flavinoid, or a nitroxide), a cytokine (IL-1, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7), or a growth factor (Flt3 ligand, c-Kit ligand, M-CSF, GM-CSF, G-CSF, VEGF, erythropoietin, leukemia inhibitory factor).

45. The method of claim 36, further comprising assessing one or more apoptotic characteristics in an HSC not treated with said caspase inhibitor.

46. A composition comprising a radioprotectant and a second agent selected from the group consisting of an anti-apoptotic molecule (a p53 inhibitor or an anti-apoptotic protein, such as Bcl-X_L, Bcl-2, c-IAP1, c-IAP2, and XIAP), a radioprotectant (amifostine, vitamin E, vitamin C, selenium, melatonin, 5-androstenediol, cucumin, α-phenyl-tert-butylnitrone, a flavinoid, or a nitroxide), a cytokine (IL-1, IL-2, IL-3, IL-4, IL-5, IL-6,

IL-7), or a growth factor (Flt3 ligand, c-Kit ligand, M-CSF, GM-CSF, G-CSF, VEGF, erythropoietin, leukemia inhibitory factor).

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